

REMARKS

Applicants thank the Examiner for withdrawing the previous rejections and for the courtesy of a telephone conversation with their Attorney on March 17, 2004.

Claims 2, 7 and 12 have not been rejected, other than for obviousness type double patenting which Applicants agree to overcome by supplying a terminal disclaimer, and Applicants respectfully submit that they are in condition for allowance.

Claim 11 has been amended to specify a list of boosters excluding damascone and alpha-ionone.

Care has been taken not to introduce any new matter.

The Present Invention

The present invention is directed to a new and unobvious combination of specified retinoids and specified retinoid boosters **in a dual compartment package, where the compartments are joined together**, intended to avoid chemical degradation of retinoids that would be caused by contact with the retinoid boosters. The specified retinoid boosters, despite boosting the effect of specified retinoids on the skin, tend to destabilize the specified retinoids in the composition. The claimed retinoid boosters are among a specific list that has been demonstrated to de-stabilize retinoids to a greater extent than the retinoids would be unstable in the absence of the boosters. Therefore, with respect to the specified retinoid boosters, there is a greater stability problem, as shown in the table on page 37 of the Specification. The retinoid/retinoid booster combinations, *both of which are intended for the same skin benefit and to be applied substantially at the same time*, are maintained in separate compartments of a package and the retinoid composition is kept out of contact with oxygen to promote its stability against chemical degradation and to avoid further instability that would be caused by contact with retinoid boosters.

The independent claims herein are further limited by dependent claims, some of which, 2, 7 and 12, are directed to retinoid combinations with *at least 2 boosters*.

A combination of a claimed retinoid (**excluding retinoic acid**) and specified boosters *mimick the effects of retinoic acid*. The effects of retinoic acid are described in the Specification and are recited in the claims. The unexpected result of the present invention is that compositions that do not contain retinoic acid behave **analogously to treatment with retinoic acid** (i.e. mimick), as if they did contain the most active form of retinoid, i.e., retinoic acid.

Claim Rejections - 35 USC § 103

Claims 1, 4-6, 9-11, 14-15 and 17-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Burger et al. (USPN 5,759,556) in view of Liu et al. (USPN 5,976,555) and further in view of Soares et al. (USPN 5,914,116). *Claim 11 has been amended to remove alpha-ionones and damascones from the listed boosters.*

According to the Office Action, Burger et al disclose a skin conditioning composition comprising a compound selected from retinol or retinyl ester in combination with *alpha-ionones and damascones*. The Office Action admits that Burger et al does not disclose the first compartment for storing retinol or retinyl ester kept out of contact with oxygen, and the second compartment for storing *alpha-ionone*, and the first and second compartments being joined together; and avoiding chemical degradation of retinol or retinyl ester in the first composition that would be caused by contact with *alpha-ionone* in the second composition.

Liu et al. is cited to supposedly remedy the deficiency for its teaching that retinal and retinyl esters quickly lose their activity and oxidize or isomerize.

Further according to the Office Action, Soares et al. (USPN 5,914,116) teaches a first and second composition stored in separate containers joined together. *However, the product of Soares et al. includes a first composition for obtaining a first skin benefit (e.g., Vitamin A palmitate) and a second composition for obtaining a second and different benefit, and the two compositions are part of a regimen teaching their application at different times of day.* The Office Action admits that Soares et al. (USPN

5,914,116) does not teach that the first and/or second compartments keep the respective compositions out of contact with oxygen, neither does it teach that the two compartments are made of aluminum, *nor does it teach the two compositions aimed at the same skin benefit and intended to be applied at substantially the same time.*

Applicants traverse this new rejection and would like to point out that that the newly cited primary reference, *Burger et al.*, does not render the present invention obvious alone or in combination with the secondary references, as discussed above, nor in combination with Granger '627. The secondary references do not remedy the deficiencies of Burger et al.

Independent claims 1, 6 and 11 relate to specific booster compounds that are shown to de-stabilize the claimed retinoids to a greater extent than the degree of instability in the absence of the boosters. See the table on page 37 of the Specification. For example, the results in the Table show that *alpha-ionone* (B1 booster) increases the rate of retinol loss by a factor of 1.3. Similarly, it can be seen that all the claimed boosters significantly increase the rate of retinol loss. Therefore, **the presence of the boosters necessitates separate compartments for the two compositions**, more so than the cited art. *These are unexpected results, not addressed by any of the cited references alone or in combination.*

Applicants respectfully submit that Liu et al. do not remedy the deficiency of *Burger et al.* Liu et al. merely restate the problem. Liu et al. merely state an invitation to invent by restating that retinoids are unstable. Liu et al. do not address the problem to which the present invention is addressed, i.e., alleviating the additional instability contributed by boosters. (At most, Liu et al. provide a different solution – i.e.

formulating in an emulsion with a specifically defined stabilizer system, but all in one composition.) The combination of *Burger et al.*, *Suares et al.* and *Liu et al.* does not arrive at the subject matter of the present invention as claimed, *and especially in Claim 11 as amended*. Although *Liu et al.* describe a container for storing the composition so that it is out of contact with oxygen, the container is described in combination with a retinoid composition with an emulsifier system and a co-emulsifier alone and does not protect the retinoid from degradation due to contact with retinoid boosters.

Accordingly, *Liu et al.* and *Suares et al.* do not remedy the deficiencies of *Burger et al.* In fact, none of the references cited in the Office Action teach or suggest the need or the solution for stabilizing retinoid compositions in the presence of retinoid enhancing actives. Therefore, although dual purpose single formulation cosmetic products have been developed in the cited art, only in hindsight, with the benefit of the disclosure of the present invention, is the need for stable cosmetic compositions that attenuate the existing problems of retinoid stability in the presence of boosters met.

Claims 3, 8 and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over *Burger et al.* (USPN 5,536,740) in view of *Suares et al.* (USPN 5,914,116) and *Liu et al.* (USPN 5,976,555) and Remington's Pharmaceutical Sciences (Remington). According to the one or more of the Office Actions, Remington in a subsection entitled "pharmaceutical containers" in the chapter on stability of pharmaceutical products teaches that aluminum containers are widely used in the pharmaceutical products.

As discussed above, *Burger et al* is an insufficient primary reference and the secondary references do not remedy its deficiencies. Furthermore, there is no motivation to combine *Burger et al* with Remington, Soares et al. and Liu et al. because Remington deals with high temperature storage. High temperature storage is not relevant to the present invention. Again, even if combined, Applicants respectfully submit that, since the independent claims are in condition for allowance, those claims that depend from them are also in condition for allowance.

Claim 16

Claim 16 specifies a booster combination of climbazole (B5) with alpha-ionone (B1) and/or damascenone.

Claim 16 was rejected under 35 U.S.C. 103(a) as being unpatentable over Burger et al in view of Granger et al. (USPN 5,716,627) in view of Soares et al. (USPN 5,914,116) and Liu et al. (USPN 5,976,555).

Granger et al disclose a skin conditioning composition comprising a) retinol or retinyl ester, b) azole, *e.g.*, *climbazole*, c) a fatty acid amide such as linoleoyl-DEA. However, as admitted in a previous Office Action, Granger et al '627 does not disclose the first compartment for storing retinol or retinyl ester kept out of contact with oxygen, and the second compartment for storing *climbazole*, and the first and second compartments being joined together; and avoiding chemical degradation of retinol or retinyl ester in the first composition that would be caused by contact with *climbazole* or *alpha ionone* in the second composition.

Applicants traverse this rejection and would like to point out that that the newly cited primary reference, Burger et al., does not render the present invention obvious either alone or in combination with the secondary references, as discussed above, nor in further combination with Granger et al '627.

As stated previously, the independent claim 11 and claim 16 dependent thereon relate to specific booster compounds that are shown to de-stabilize the claimed retinoids to a greater extent than the degree of instability in the absence of the boosters. See the table on page 37 of the Specification. For example, the results in the Table show that *alpha-ionone* increases the rate of retinol loss by a factor of 1.3. Similarly, it can be seen that all the claimed boosters significantly increase the rate of retinol loss. Therefore, the **presence of the boosters necessitates separate compartments for the two compositions**, more so than the cited art. *These are unexpected results.*

Applicants respectfully submit that Liu et al. do not remedy the deficiency of Granger et al '627. Firstly, Liu et al. merely restate the problem. Liu et al. merely state an invitation to invent by restating that retinoids are unstable. Liu et al. do not address the problem to which the present invention is addressed, i.e., alleviating the additional instability contributed by boosters. (At most, Liu et al. provide a different solution – i.e. formulating in an emulsion with a specifically defined stabilizer system, but all in one composition.) Secondly, the combination of Granger et al '627, Soares et al. and Liu et al. does not arrive at the subject matter of the present invention as claimed in Claims 1, 6 and 11, as amended. Although Liu et al. describe a container for storing the composition so that it is out of contact with oxygen, the container is described in combination with a retinoid composition with an emulsifier system and a co-emulsifier

alone and does not protect the retinoid from degradation due to contact with retinoid boosters.

Granger et al '627 do not remedy the deficiencies of Burger et al., Liu et al., and Suares. If fact, none of the references cited in the Office Action teach or suggest the need or the solution for stabilizing retinoid compositions in the presence of retinoid enhancing actives. Therefore, although dual purpose single formulation cosmetic products have been developed in the cited art, only in hindsight, with the benefit of the disclosure of the present invention, is the need for stable cosmetic compositions that attenuate the existing problems of retinoid stability in the presence of boosters met. Even if combined, Applicants respectfully submit that, since the independent claims are in condition for allowance, those claims that depend from them are also in condition for allowance.

An obviousness rejection is proper only when “the subject matter as a whole would have been obvious at the time the invention was made ...” (emphasis added). 35 U.S.C. 103. Applicants respectfully submit that the Office Action has improperly chosen certain aspects of one reference and combined them with aspects of other references, without showing where the motivation is to combine them to come up with the subject matter of the present invention as a whole, within the meaning of 35 U.S.C. 103. Applicants submit that the pending claims are not obvious over the cited references, under 35 U.S.C. 103, especially in view of the present Amendment. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections –Double Patenting

Applicants traverse these rejections. Applicants respectfully maintain that the double patenting rejections under the judicially created doctrine of obviousness-type double patenting is improper for the reasons discussed above. Additionally, as the primary purpose of the double patenting doctrine is to prevent an extension of the statutory period of monopoly that would occur if successive patents were allowed *on the same basic concept*, the fact that this rejection requires multiple references, many of which are not Applicants', indicates that the patents are not for the same invention or for an obvious modification of the same invention. The inventions are not for the same basic concept and the obviousness type double patenting rejections are therefore traversed. Nevertheless, in the interest of progressing the present application to issue without delay, to the extent any double patenting rejections may remain, Applicants would be willing to supply a terminal disclaimer upon indication of allowability of the present claims.

In view of the foregoing amendments and comments, Applicants request the Examiner to reconsider the rejection and now allow the claims.

Respectfully submitted,



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